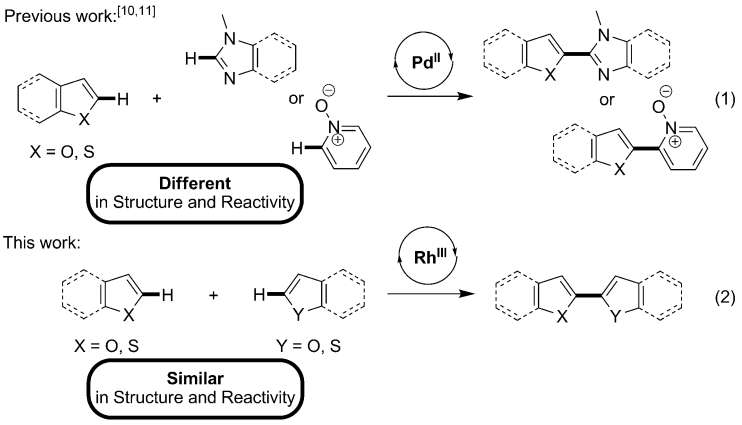
C–H Activation

DOI: 10.1002/anie.201203792

Selective Rhodium(III)-Catalyzed Cross-Dehydrogenative Coupling of Furan and Thiophene Derivatives**

*Nadine Kuhl, Matthew N. Hopkinson, and Frank Glorius**

The cross-dehydrogenative coupling (CDC) of two unfunctionalized arenes is one of the most attractive transformations to build up the ubiquitous biaryl motif.[1,2] In comparison to established cross-coupling reactions between aryl halides and organometallic reagents,[3] CDC is considered a more efficient and environmentally friendly approach since it circumvents the often tedious and wasteful pre-functionalization of starting materials. However, the use of C–H bonds as functional groups in these reactions raises substantial challenges. Besides reactivity and regioselectivity, a major challenge is to control the reaction pathway such that the cross-coupling product is favored over undesired homocoupling pathways.[4]



In the last few years, several studies describing the CDC of, for example, one arene decorated with a directing group and one simple arene,[5] the coupling between two simple arenes,[6] and the arylation of heterocycles[7] have been reported. In comparison, the cross-dehydrogenative coupling of two heteroarenes is surprisingly under-represented despite the high value of the resulting bi(heteroarene) products in medicinal chemistry and materials science.[8,9] First reports on palladium-catalyzed couplings between electron-rich heteroarenes and electron-deficient N-containing heterocycles, such as azoles and pyridine N-oxides, were disclosed by You et al.[10] and Itami et al.[11] [Eq. (1)]. Concurrently, Ofial and co-workers also demonstrated that very similar azole heterocycles undergo efficient C–H/C–H bond coupling.[12] Several oxazoles, thiazoles, and imidazoles were shown to selectively cross-couple at their C2-positions with various benzannulated azoles.[12] Similarly, You et al. revealed that this transformation is even feasible for two structurally similar azoles.[13] However, a chemo- and regioselective transition-metal-catalyzed CDC of two similar heterocycles other than azoles, in particular of furans, thiophenes, and pyrroles, has not been accomplished to date.[14,15]

Rhodium(III)-catalyzed reactions[16] of arenes with olefins,[17] alkynes,[18] allenes,[19] carbon monoxide,[20] chloroamines,[21] or carbonyl compounds[22] have been studied over the last few years. However, the Rhodium(III)-catalyzed formation of biaryls by C–H/C–H coupling has remained unprecedented.[23,24] Recently it was demonstrated that $[\{RhCp^*Cl_2\}_2]$ ($Cp^* = C_5Me_5$) is also a suitable catalyst for the intermolecular CDC of benzamides and haloarenes to afford halogenated biaryl compounds with high levels of chemo- and regioselectivity.[25]

Herein, we report the successful application of $[\{RhCp^*Cl_2\}_2]$ to the dehydrogenative coupling of structurally similar furan and thiophene heterocycles, affording coupled products featuring the 2,2′-bi(heteroaryl) motif which is prominent in semiconducting materials[26] and biologically active compounds.[27] These reactions proceed with excellent regiocontrol whilst high selectivity for the cross-coupled products was generally observed [Eq. (2)]. Furthermore, the methodology could also be extended to sensitive indole and pyrrole coupling partners.[28]

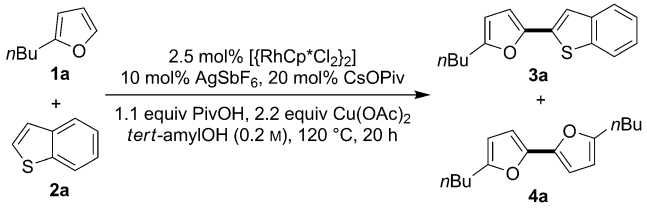
The CDC of 2-*n*-butylfuran (**1a**) and benzothiophene (**2a**) was selected as the model transformation as this system allows for facile analysis of the reaction by ^{1}H NMR spectroscopy. Starting from our previously reported conditions, $[\{RhCp^*Cl_2\}_2]$ (2.5 mol%), $AgSbF_6$ (10 mol%), CsOPiv (20 mol%), PivOH (1.1 equiv), and $Cu(OAc)_2$ (2.2 equiv),[25] an initial solvent screen revealed *tert*-AmylOH to be superior, delivering the desired cross-coupled product **3a** in 47% NMR yield along with 18% of 2,2′-bi(furan) **4a** resulting from homocoupling of **1a** (Table 1, entry 1). Interestingly, no homocoupling of **2a** was observed even though this component was used in slight excess

[*] N. Kuhl, Dr. M. N. Hopkinson, Prof. Dr. F. Glorius
Organisch-Chemisches Institut
Westfälische Wilhelms-Universität Münster
Corrensstrasse 40, 48149 Münster (Germany)
E-mail: glorius@uni-muenster.de
Homepage: http://www.uni-muenster.de/Chemie.oc/glorius/en/

[**] We thank A. Rühling and C. Weitkamp for great experimental support. Generous financial support by the European Research Council under the European Community's Seventh Framework Program (FP7 2007–2013)/ERC Grant agreement no. 25936, the Alfried Krupp von Bohlen and Halbach Foundation, and the Fonds der Chemischen Industrie (N.K.) is gratefully acknowledged.

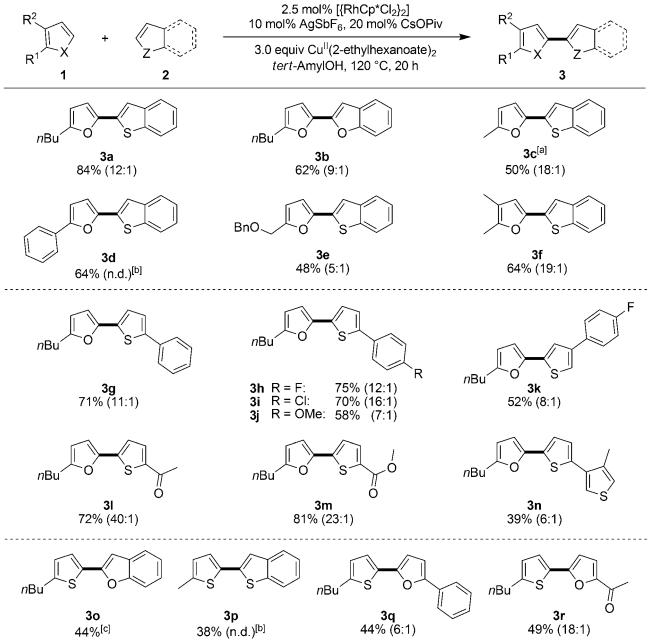
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201203792.

Table 1: Optimization.[a]



Entry	**1a**:**2a**	Variation	Yield **3a** [%][b]	**3a**:**4a**[c]
1	1:1.5	no variation	47	3:1
2	1:1.5	20 mol% PivOH	33	2:1
3	1:3	no variation	59	7:1
4	1:3	AcOH	16	2:1
5	1:3	2.2 equiv Cu_2O	32	6:1
6	1:3	2.2 equiv $Cu(OH)_2$	36	9:1
7	1:3	2.2 equiv **5**	68	17:1
8	1:3	no PivOH, 2.2 equiv **5**	69 (71)	11:1
9	**1:3**	**no PivOH, 3.0 equiv 5**	**85 (84)**	**12:1**
10	1:3	no $[RhCp^*Cl_2]_2$[d]	n.r.	–
11	1:3	no $AgSbF_6$[d]	74	12:1
12	1:3	no CsOPiv[d]	n.r.	–

[a] Reactions were performed on a 0.2 mmol scale, best result highlighted in bold. [b] The yield was determined by ^{1}H NMR spectroscopy of the crude product using CH_2Br_2 as an internal standard. Yields of isolated products are given in brackets. [c] The **3a**:**4a** ratio (based on conversion of **1a**) was determined by ^{1}H NMR spectroscopy of the crude product mixture. [d] 3.0 equiv of **5** was used. **5**: Cu^{II}(2-ethylhexanoate)$_2$.



Scheme 1. Substrate scope. Yields of isolated products are given. **3**:**4** ratios based on **1**, given in brackets, were determined by ^{1}H NMR spectroscopy of the crude product mixture if possible. General reaction conditions: **1** (0.5 mmol), **2** (1.5 mmol), $[\{RhCp^*Cl_2\}_2]$ (2.5 mol%), $AgSbF_6$ (10 mol%), CsOPiv (20 mol%), Cu^{II}(2-ethylhexanoate)$_2$ (3.0 equiv), *tert*-AmylOH (2.0 mL), 120°C, 20 h. [a] Reaction was performed on a 0.4 mmol scale. [b] Determination of the **3**:**4** ratio by ^{1}H NMR spectroscopy was not possible. [c] No homocoupling of **1o**.

(1.5 equiv). Moreover the 2,2′-cross-coupled product was obtained as a single regioisomer with C–H functionalization occurring exclusively at the C2-position of both the furan and the benzothiophene components. Despite screening of various parameters, only an increased amount of **2a** (3 equiv) could improve the yield of **3a** significantly (59%, entry 3). Further variations of the reaction conditions, such as doubling the catalyst loading or increasing the reaction time failed to improve the reaction outcome.[29,30] We hypothesized that acetic acid generated in situ from $Cu(OAc)_2$ could possibly hamper the coupling process and consequently tested a range of different Cu^{II} oxidants.[31] Whilst salts with more basic counteranions were less effective (entries 5 and 6), commercially available Cu^{II}(2-ethylhexanoate)$_2$ (**5**) improved the yield to 68% (entry 7). In this case, addition of pivalic acid became unnecessary (entry 2 vs. entry 8). Increasing the amount of oxidant to 3 equivalents delivered **3a** isolated in 84% yield with a respectable 12:1 selectivity for the cross-coupled product over the furan homodimer **4a** (entry 9). Control reactions performed in the absence of the rhodium or silver precatalysts revealed that, whilst Rh^{III} was essential for the coupling process, **3a** was also produced in the absence of $AgSbF_6$, albeit with slightly lower efficiency (entries 10 and 11).

With the optimized conditions in hand, we sought to investigate the generality of the CDC process with other substrate combinations. To our delight, 2-*n*-butylfuran (**1a**) also underwent efficient coupling with benzofuran **2b**, affording **3b**, isolated in 62% yield (Scheme 1). Again in this case, good selectivity for the cross-coupled product over the furan homodimer **4a** was achieved (ratio **3b**:**4a** 9:1), whilst no products resulting from homocoupling of the benzofuran component could be isolated from the reaction mixture. Moreover, exclusive formation of the 2,2′-bi(heteroarene) regioisomer was observed. A selection of various 2-alkyl and 2-aryl substituted furans (**3a**–**3e**) reacted smoothly with benzothiophene **2a** under the standard conditions whilst the 2,3-disubstitution pattern was also tolerated (**3f**).

The range of coupling partners amenable to CDC with furans was not limited to benzannulated derivatives. Substrate **1a** was efficiently arylated with various 2-aryl thiophenes in good yields and high chemo- and regioselectivities (**3g–3j**). In addition, a 3-substituted thiophene could also be employed leading to product **3k** in 52% yield as a single regioisomer.[32] Similarly, 2,3′-bi(thiophene) **2n** bearing a 2,5-unsubstituted thiophene moiety yielded only one cross-coupling product (**3n**). Importantly, several synthetically valuable functional groups, such as halides (**3h**, **3i**), ketones (**3l**), and esters (**3m**), were tolerated under the reaction conditions delivering the desired cross-coupled products in excellent yields and regioselectivities (e.g. **3l** 72%, **3m** 81%).[33]

Finally, 2-alkyl-substituted thiophenes could also be successfully employed in place of the furan component, leading to various 2-heteroarylthiophenes in moderate yields (**3o–3r**).

In general, more efficient coupling was observed between substrates with different electronic profiles. For example, the

comparatively electron-deficient 2-acetylfuran did not react with benzothiophene **2a** but did couple with the more electron-rich 2-*n*-butylthiophene (**3r**, 49%). In contrast, the reaction between **1a** and 2-methylthiophene lead to an inseparable mixture of the cross-coupled product and significant amounts of both homo-coupled products (**3**:**4** ratio 2:1).[29]

With the observation that more electron-rich furans or thiophenes tend to undergo selective coupling preferentially with a rather electron-poor partner, we assumed that alkyl-substituted furans or thiophenes could be replaced with electron-rich N-heterocycles. Indeed, after a short screening of suitable protecting groups, *N*-benzylindole was found to couple with benzothiophene **2a** and benzofuran **2b** yielding the desired products **6a** and **6b** in 39% and 62% yield, respectively. Intriguingly, excellent selectivity for the indole C3-position was observed in both cases (Figure 1). Moreover, benzyl protected 2-acetylpyrrole could also be converted into the corresponding biaryl **7** in 44% yield with coupling again occurring preferentially at the C3-position.[34]

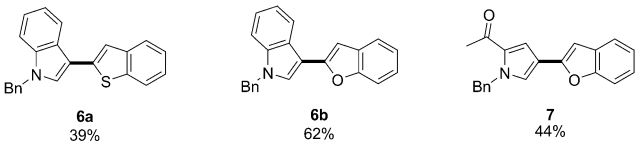


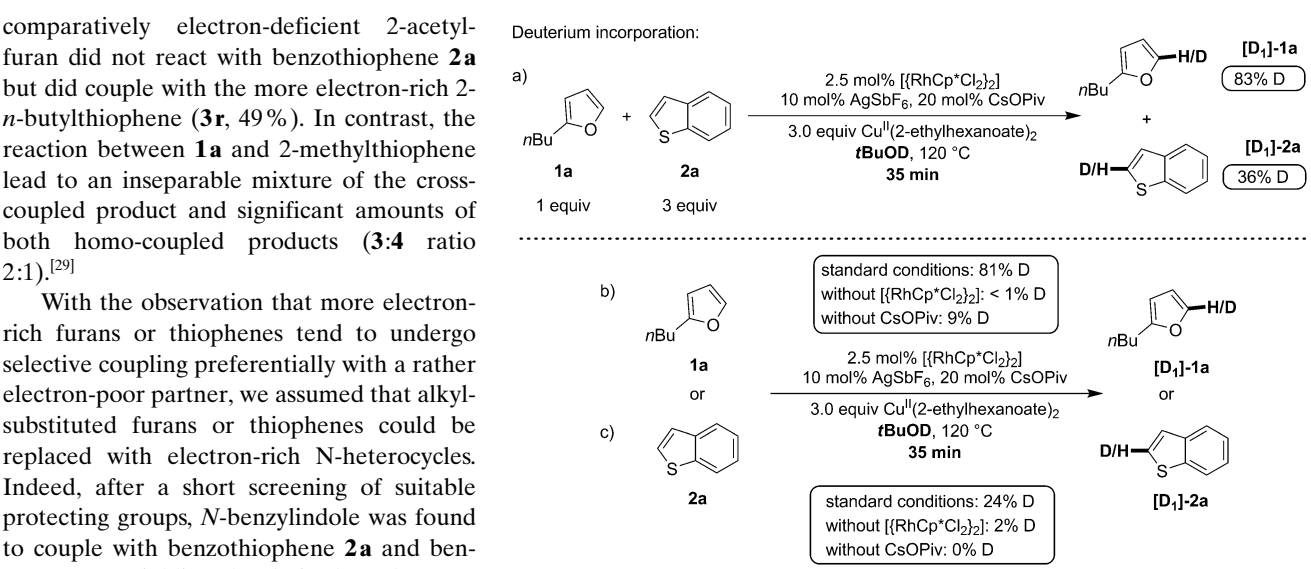
Figure 1. Coupling products and yields of isolated products for the reactions of *N*-benzylindole and *N*-benzyl-2-acetylpyrrole with benzofuran and/or benzothiophene.[34]

With the scope and limitations of the CDC process established, our attention turned to an investigation of the reaction mechanism. Firstly, deuterium labeling experiments for the standard reaction between **1a** and **2a** and for each coupling partner (**1a** or **2a**) in isolation were performed. When the standard reaction was conducted in *t*BuOD for 35 min at 120 °C, significant deuterium incorporation in both partners, **1a** (83% D) and **2a** (36% D) was observed (Scheme 2a).[35]

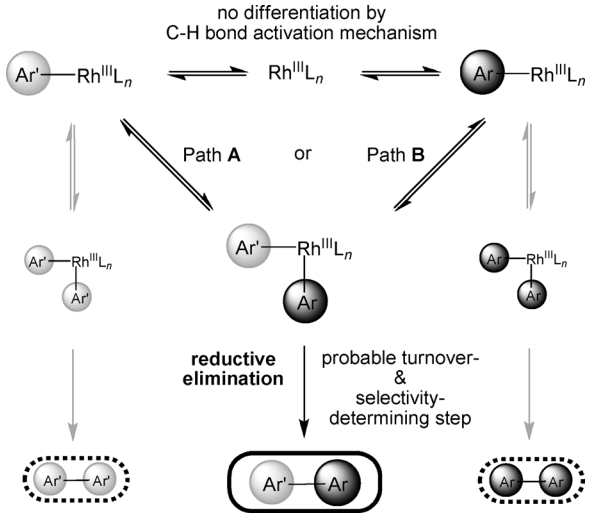
Moreover, a similar outcome was obtained when the coupling partners were exposed to the same reaction conditions in the absence of the other component (**1a** (81% D), **2a** (24% D)), indicating that C–H activation of both reactants is reversible and largely independent of the presence of the other coupling partner (Scheme 2b,c). Notably, the corresponding control experiments without the Rh^{III} precatalyst or without CsOPiv did not result in considerable deuterium incorporation in **1a** or **2a**, implying that a similar Rh^{III}/CsOPiv-mediated C–H activation mechanism is operating for both coupling partners.[36]

Furthermore, initial rate measurements revealed kinetic isotope effects (KIEs) of 0.9 and 1.3 for **1a** and **2a**, respectively, indicating that C–H bond cleavage at either coupling partner is not necessarily involved in the turnover limiting step of the catalytic cycle.[37] Instead, reductive elimination from a potential diaryl rhodium(III) species may be both the turnover and also the selectivity determining step in the catalytic cycle. Additionally, reversibility of the furan C–H activation and the excess of the less reactive coupling partner **2a** (**1a**:**2a** 1:3) seem to be key factors controlling selectivity for the cross-coupling product since running the reaction only with **1a** (i.e. without **2a**) generates homocoupling product **4a** in a considerable yield of 58%. Despite these results, the true order of C–H activation events in the catalytic cycle remains a point of discussion (Scheme 3).[38]

In summary, we have developed the first rhodium(III)-catalyzed cross-dehydrogenative coupling (CDC) of furans with benzothiophenes and thiophenes leading to the corre-



Scheme 2. Deuterium labeling experiments.



Scheme 3. Mechanistic scheme for the CDC process consistent with the preliminary mechanistic results.

sponding 2,2′-bi(heteroaryl) compounds in good yields and excellent regioselectivities. High levels of selectivity for the cross-coupled products over homodimers of either coupling partner were generally observed. Additionally, the reaction conditions could also be applied to other substrate combinations including indoles and pyrroles. Furthermore, we believe that the apparent ability of Rh^{III} to regioselectively activate heteroaromatic C–H bonds demonstrated herein could pave the way for the development of many novel coupling reactions involving a wide range of different heterocycles.

Received: May 16, 2012
Published online: ■■ ■■, ■■■■

Keywords: cross-dehydrogenative coupling · heterobiaryls · heterocycles · rhodium · selectivity

[1] C–H activation Reviews: a) T. Newhouse, P. S. Baran, *Angew. Chem.* **2011**, *123*, 3422 – 3435; *Angew. Chem. Int. Ed.* **2011**, *50*, 3362 – 3374; b) L. Ackermann, *Chem. Rev.* **2011**, *111*, 1315 – 1345; c) L. McMurray, F. O'Hara, M. J. Gaunt, *Chem. Soc. Rev.* **2011**, *40*, 1885 – 1898; d) C. S. Yeung, V. M. Dong, *Chem. Rev.* **2011**, *111*, 1215 – 1292; e) J. Wencel-Delord, T. Dröge, F. Liu, F. Glorius, *Chem. Soc. Rev.* **2011**, *40*, 4740 – 4761; f) D. A. Colby, R. G. Bergman, J. A. Ellman, *Chem. Rev.* **2010**, *110*, 624 – 655; g) T. W. Lyons, M. S. Sanford, *Chem. Rev.* **2010**, *110*, 1147 – 1169; h) L. Ackermann, R. Vicente, A. R. Kapdi, *Angew. Chem.* **2009**, *121*, 9976 – 10011; *Angew. Chem. Int. Ed.* **2009**, *48*, 9792 – 9826.

[2] Recent Reviews on cross-coupling of unfunctionalized arenes: a) J. A. Ashenhurst, *Chem. Soc. Rev.* **2010**, *39*, 540 – 548; b) A. Lei, W. Liu, C. Liu, M. Chen, *Dalton Trans.* **2010**, *39*, 10352 – 10361; c) S.-L. You, J.-B. Xia, *Top. Curr. Chem.* **2010**, *292*, 165 – 194.

[3] *Metal-catalyzed Cross-Coupling Reactions*, *2nd ed.* (Eds.: A. de Meijere, F. Diederich), Wiley-VCH, Weinheim, **2004**.

[4] For site-selective C–H activation, see: S. R. Neufeldt, M. S. Sanford, *Acc. Chem. Res.* **2012**, *45*, 936 – 946.

[5] a) J. Wencel-Delord, C. Nimphius, F. W. Patureau, F. Glorius, *Angew. Chem.* **2012**, *124*, 2290 – 2294; *Angew. Chem. Int. Ed.* **2012**, *51*, 2247 – 2251; b) X. Wang, D. Leow, J.-Q. Yu, *J. Am. Chem. Soc.* **2011**, *133*, 13864 – 13867; c) T. W. Lyons, K. L. Hull, M. S. Sanford, *J. Am. Chem. Soc.* **2011**, *133*, 4455 – 4464; d) X. Zhao, C. S. Yeung, V. M. Dong, *J. Am. Chem. Soc.* **2010**, *132*, 5837 – 5844; e) S. H. Cho, S. J. Hwang, S. Chang, *J. Am. Chem. Soc.* **2008**, *130*, 9254 – 9256; f) B.-J. Li, S.-L. Tian, Z. Fang, Z.-J. Shi, *Angew. Chem.* **2008**, *120*, 1131 – 1134; *Angew. Chem. Int. Ed.* **2008**, *47*, 1115 – 1118; g) G. Brasche, J. García-Fortanet, S. L. Buchwald, *Org. Lett.* **2008**, *10*, 2207 – 2210.

[6] a) L. Zhou, W. Lu, *Organometallics* **2012**, *31*, 2124 – 2127; b) H. Li, C.-L. Sun, B.-J. Li, Z.-J. Shi, *Org. Lett.* **2011**, *13*, 276 – 279; c) Y. Wie, W. Su, *J. Am. Chem. Soc.* **2010**, *132*, 16377 – 16379; d) R. Li, L. Jiang, W. Lu, *Organometallics* **2006**, *25*, 5973 – 5975; for intramolecular CDC, see: e) D. G. Pintori, M. F. Greaney, *J. Am. Chem. Soc.* **2011**, *133*, 1209 – 1211; f) L. Ackermann, R. Jeyachandran, H. K. Potukuchi, P. Novák, L. Büttner, *Org. Lett.* **2010**, *12*, 2056 – 2059.

[7] For the arylation of indoles, see: a) S. Potavathri, K. C. Pereira, S. I. Gorelsky, A. Pike, A. P. LeBris, B. DeBoef, *J. Am. Chem. Soc.* **2010**, *132*, 14676 – 14681; b) D. R. Stuart, K. Fagnou, *Science* **2007**, *316*, 1172 – 1175; c) D. R. Stuart, E. Villemure, K. Fagnou, *J. Am. Chem. Soc.* **2007**, *129*, 12072 – 12073; for other heterocycles, see: d) C.-Y. He, Q.-Q. Min, X. Zhang, *Organometallics* **2012**, *31*, 1335 – 1340; e) C. C. Malakar, D. Schmidt, J. Conrad, U. Beifuss, *Org. Lett.* **2011**, *13*, 1378 – 1381; f) C.-Y. He, S. Fan, X. Zhang, *J. Am. Chem. Soc.* **2010**, *132*, 12850 – 12852.

[8] For selected Reviews on the C–H activation of heterocycles, see: a) S. H. Cho, J. Y. Kim, J. Kwak, S. Chang, *Chem. Soc. Rev.* **2011**, *40*, 5068 – 5083; b) K. Hirano, M. Miura, *Synlett* **2011**, 294 – 307; c) D. Zhao, J. You, C. Hu, *Chem. Eur. J.* **2011**, *17*, 5466 – 5492; d) K. Fagnou, *Top. Curr. Chem.* **2010**, *292*, 35 – 56; e) E. M. Beck, M. J. Gaunt, *Top. Curr. Chem.* **2010**, *292*, 85 – 121.

[9] Recent Highlights on cross-coupling of heterocycles: a) X. Bugaut, F. Glorius, *Angew. Chem.* **2011**, *123*, 7618 – 7620; *Angew. Chem. Int. Ed.* **2011**, *50*, 7479 – 7481; b) W. Han, A. R. Ofial, *Synlett* **2011**, 1951 – 1955.

[10] a) Z. Wang, K. Li, D. Zhao, J. Lan, J. You, *Angew. Chem.* **2011**, *123*, 5477 – 5481; *Angew. Chem. Int. Ed.* **2011**, *50*, 5365 – 5369; b) P. Xi, F. Yang, S. Qin, D. Zhao, J. Lan, G. Gao, C. Hu, J. You, *J. Am. Chem. Soc.* **2010**, *132*, 1822 – 1824.

[11] a) A. D. Yamaguchi, D. Mandal, J. Yamaguchi, K. Itami, *Chem. Lett.* **2011**, *40*, 555 – 557; b) D. Mandal, A. D. Yamaguchi, J. Yamaguchi, K. Itami, *J. Am. Chem. Soc.* **2011**, *133*, 19660 – 19663.

[12] W. Han, P. Mayer, A. R. Ofial, *Angew. Chem.* **2011**, *123*, 2226 – 2230; *Angew. Chem. Int. Ed.* **2011**, *50*, 2178 – 2182.

[13] J. Dong, Y. Huang, X. Qin, Y. Cheng, J. Hao, D. Wan, W. Li, X. Liu, J. You, *Chem. Eur. J.* **2012**, *18*, 6158 – 6162.

[14] Metal-free arylation of thiophenes: Y. Kita, K. Morimoto, M. Ito, C. Ogawa, A. Goto, T. Dohi, *J. Am. Chem. Soc.* **2009**, *131*, 1668 – 1669.

[15] Copper-catalyzed iodination/arylation sequence: H.-Q. Do, O. Daugulis, *J. Am. Chem. Soc.* **2011**, *133*, 13577 – 13586.

[16] For an overview on Rh^{III}-catalyzed C–H activation reactions, see: a) G. Song, F. Wang, X. Li, *Chem. Soc. Rev.* **2012**, *41*, 3651 – 3678; b) T. Satoh, M. Miura, *Chem. Eur. J.* **2010**, *16*, 11212 – 11222; c) F. W. Patureau, J. Wencel-Delord, F. Glorius, *Aldrichimica Acta* **2012**, *45*, 31 – 41.

[17] For selected examples of Rh^{III}-catalyzed oxidative Heck reactions see: a) S. Mochida, K. Hirano, T. Satoh, M. Miura, *J. Org. Chem.* **2011**, *76*, 3024 – 3033; b) X. Li, M. Zhao, *J. Org. Chem.* **2011**, *76*, 8530 – 8536; c) S. H. Park, J. Y. Kim, S. Chang, *Org. Lett.* **2011**, *13*, 2372; d) A. S. Tsai, M. Brasse, R. G. Bergman, J. A. Ellman, *Org. Lett.* **2011**, *13*, 540 – 542; e) F. Wang, G. Song, Z. Du, X. Li, *J. Org. Chem.* **2011**, *76*, 2926 – 2932; f) F. W. Patureau, T. Besset, F. Glorius, *Angew. Chem.* **2011**, *123*, 1096 – 1099; *Angew. Chem. Int. Ed.* **2011**, *50*, 1064 – 1067; g) F. W. Patureau, C. Nimphius, F. Glorius, *Org. Lett.* **2011**, *13*, 6346 – 6349; h) K. Ueura, T. Satoh, M. Miura, *Org. Lett.* **2007**, *9*, 1407 – 1409.

[18] For selected examples of Rh^{III}-catalyzed annulation reactions with alkynes see: a) B.-J. Li, H.-Y. Wang, Q.-L. Zhu, Z.-J. Shi, *Angew. Chem.* **2012**, *124*, 4014 – 4018; *Angew. Chem. Int. Ed.* **2012**, *51*, 3948 – 3952; b) T. Fukutani, K. Hirano, T. Satoh, M. Miura, *J. Org. Chem.* **2011**, *76*, 2867 – 2874; c) N. Guimond, S. I. Gorelsky, K. Fagnou, *J. Am. Chem. Soc.* **2011**, *133*, 6449 – 6457; d) F. W. Patureau, T. Besset, N. Kuhl, F. Glorius, *J. Am. Chem. Soc.* **2011**, *133*, 2154 – 2156; e) T. K. Hyster, T. Rovis, *Chem. Commun.* **2011**, *47*, 11846 – 11848; f) N. Umeda, H. Tsurugi, T, Satoh, M. Miura, *Angew. Chem.* **2008**, *120*, 4083 – 4086; *Angew. Chem. Int. Ed.* **2008**, *47*, 4019 – 4022.

[19] H. Wang, F. Glorius, *Angew. Chem.* **2012**, DOI: 10.1002/ange.201201273; *Angew. Chem. Int. Ed.* **2012**, DOI: 10.1002/anie.201201273.

[20] Y. Du, T. K. Hyster, T. Rovis, *Chem. Commun.* **2011**, *47*, 12074 – 12076.

[21] a) C. Grohmann, H. Wang, F. Glorius, *Org. Lett.* **2012**, *14*, 656 – 659; b) K.-H. Ng, Z. Zhou, W.-Y. Yu, *Org. Lett.* **2012**, *14*, 272 – 275.

[22] Selected Rh^{III}-catalyzed additions to electrophiles: a) N. Schröder, J. Wencel-Delord, F. Glorius, *J. Am. Chem. Soc.*

2012, *134*, 8298 – 8301; b) Y. Li, X.-S. Zhang, H. Li, W.-H. Wang, K. Chen, B.-J. Li, Z.-J. Shi, *Chem. Sci.* **2012**, *3*, 1634 – 1639; c) M. E. Tauchert, C. D. Incarvito, A. L. Rheingold, R. G. Bergman, J. A. Ellman, *J. Am. Chem. Soc.* **2012**, *134*, 1482 – 1485; d) K. D. Hesp, R. G. Bergman, J. A. Ellman, *J. Am. Chem. Soc.* **2011**, *133*, 11430 – 11433.

[23] For a Rh^{III}-catalyzed biaryl formation, see: A. G. M. Barrett, T. Itoh, E. M. Wallace, *Tetrahedron Lett.* **1993**, *34*, 2233 – 2234; however, this transformation probably does not involve C–H bond activation.

[24] Selected references for C–H activation reactions using Rh^{I} precatalysts: a) J. C. Lewis, R. G. Bergman, J. A. Ellman, *Acc. Chem. Res.* **2008**, *41*, 1013 – 1325; b) S. Yanagisawa, T. Sudo, R. Noyori, K. Itami, *Tetrahedron* **2008**, *64*, 6073 – 6081; c) S. Yanagisawa, T. Sudo, R. Noyori, K. Itami, *J. Am. Chem. Soc.* **2006**, *128*, 11748 – 11749; d) X. Wang, B. S. Lane, D. Sames, *J. Am. Chem. Soc.* **2005**, *127*, 4996 – 4997. From Rh^{II}: e) J. Kwak, M. Kim, S. Chang, *J. Am. Chem. Soc.* **2011**, *133*, 3780 – 3783.

[25] a) see Ref. [5a]; b) J. Wencel-Delord, C. Nimphius, F. W. Patureau, F. Glorius, *Chem. Asian J.* **2012**, *7*, 1208 – 1212; for a recent intramolecular aryl – aryl coupling by CDC, see: c) K. Morimoto, M. Ioh, K. Hirano, T. Satoh, Y. Shibata, K. Tanaka, M. Miura, *Angew. Chem.* **2012**, *124*, 5455 – 5458; *Angew. Chem. Int. Ed.* **2012**, *51*, 5359 – 5362.

[26] For selected Reviews, see: a) P. M. Beaujuge, J. R. Reynolds, *Chem. Rev.* **2010**, *110*, 268 – 320; b) W. Wu, Y. Liu, D. Zhu, *Chem. Soc. Rev.* **2010**, *39*, 1489 – 1502.

[27] Selected example: J. Yang, A. Ahmed, E. Poon, N. Perusinghe, A. de Haven Brandon, G. Box, M. Valenti, S. Eccles, K. Rouschop, B. Wouters, M. Ashcroft, *Mol. Cell. Biol.* **2009**, *29*, 2243 – 2253.

[28] A Rh^{III}-catalyst was recently applied in the acylation of indoles: B. Zhou, Y. Yang, Y. Li, *Chem. Commun.* **2012**, *48*, 5163 – 5165.

[29] For more details see the Supporting Information.

[30] Poisoning of the catalyst by **3a** or **3q** can be excluded. See Supporting Information.

[31] Among other oxidants, Cu^{II} salts proved to be superior. See the Supporting Information.

[32] The regioselectivity of the C–H activation seemed to be strongly influenced by steric effects, that is, only trace product was observed in the reaction between 3-methyl benzothiophene with 2-*n*-butylfuran.

[33] The use of simple furan or thiophene led to oligomerization.

[34] The product constitution was verified by NMR spectroscopy. See the Supporting Information.

[35] The standard reaction in *t*BuOH gave **3a** in 79% ^{1}H NMR yield with a **3a**:**4a** ratio of 11:1.

[36] A concerted metalation-deprotonation (CMD) mechanism was calculated to be favorable for the palladium-catalyzed C–H activation of various heterocycles: a) S. I. Gorelsky, D. Lapointe, K. Fagnou, *J. Am. Chem. Soc.* **2008**, *130*, 10848 – 10849; b) S. I. Gorelsky, D. Lapointe, K. Fagnou, *J. Org. Chem.* **2012**, *77*, 658 – 668; similar calculations have not yet been performed for Rh^{III}. However, C–H activation via a CMD mechanism would explain the observed regioselectivity.

[37] E. M. Simmons, J. F. Hartwig, *Angew. Chem.* **2012**, *124*, 3120 – 3126; *Angew. Chem. Int. Ed.* **2012**, *51*, 3066 – 3072.

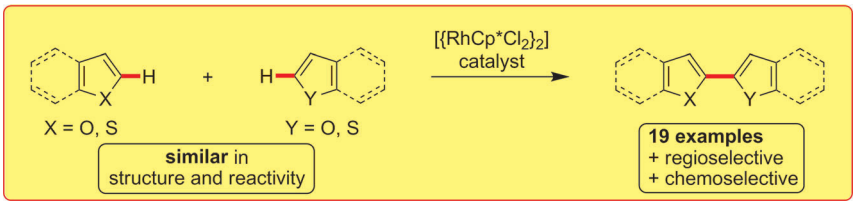
[38] For an insightful theoretical work on the cross-coupling of indole and benzene: R. Meir, S. Kozuch, A. Uhe, S. Shaik, *Chem. Eur. J.* **2011**, *17*, 7623 – 7631.

Communications

C–H Activation

N. Kuhl, M. N. Hopkinson,
F. Glorius* ——————— ■■■■–■■■■

Selective Rhodium(III)-Catalyzed Cross-Dehydrogenative Coupling of Furan and Thiophene Derivatives



A hot couple: An unprecedented rhodium(III)-catalyzed cross-dehydrogenative coupling (CDC) of various furan and thiophene derivatives leads to valuable 2,2′-bi(heteroaryl) products in good yields and selectivities (see scheme). In addition, pyrroles and indoles can also be used as coupling partners, giving C3-arylated products.